

## REMARKS

Upon entry of the foregoing amendment, claims 1, 2, 5, and 9-17 are pending in the application, with claims 1, 2, and 15 being the independent claims. Claims 1, 2, and 9-14 are sought to be amended. New claims 15-17 are sought to be added. Claims 3, 4, and 8 are sought to be cancelled by the present amendment without prejudice to or disclaimer of the subject matter therein. Claims 6 and 7 were cancelled by previous amendment.

Claim 1 has been amended to recite the compounds of Examples 1-5. Support for this change can be found in the specification as filed, at pages 6-10. Claim 2 has been amended into independent format and to incorporate the definitions of variables  $R_1$ - $R_3$  and  $n$  of Formula I recited in the previous version of claim 1, from which it originally depended. Claim 9 has been amended to delete the compound 8-fluoro-isoquinoline-3-carboxylic acid {(S)-1-azabicyclo[2.2.2]oct-2-yl}-amide.

Claims 9-14 have also been amended to correct a typographical error in the chemical name of each compound by replacing “oct-2-yl” with “oct-3-yl,” to correctly signify that in each compound, the point of attachment of the 1-azabicyclo[2.2.2]octyl moiety to the remainder of the molecule is at C3 (ring atom #3) of the 1-azabicyclo[2.2.2]octyl ring, rather than at C2 (ring atom #2). Applicant believes that this change is clearly supported by Formula I in the specification, which indicates that C3 of the azabicyclo[2.2.2]octyl moiety is connected to the amide nitrogen of the isoquinoline-3-carboxamide moiety.

Support for new claims 15-17 can be found in the specification as originally filed, in Examples 1-5, at pages 6-10, and in original claims 2 and 5.

These changes are believed to introduce no new matter, and their entry is respectfully requested. Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

### **I. Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph**

Claim 8 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. (Office Action, at page 2, lines 14-17.)

To expedite prosecution and without acquiescing to the propriety of the rejection, Applicant has cancelled claim 8, rendering the rejection moot.

Accordingly, Applicant requests that the rejection of claim 8 under 35 U.S.C. § 112, first paragraph, be withdrawn.

## **II. Rejection of the Claims Under 35 U.S.C. § 102**

Claims 1, 3-5, and 8 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Jacobsen *et al.*, U.S. Pat. No. 7,001,900 (“Jacobsen”). (Office Action, at page 6, lines 17-19.) In support of the rejection, the Office cites a number of specific isoquinoline-substituted bicyclo compounds disclosed in Jacobsen. (Office Action, at pages 6-12.)

Claims 3, 4 and 8 have been cancelled, rendering the rejection moot with respect to these claims.

With respect to claims 1 and 5, to expedite prosecution and without acquiescing to the propriety of the rejection, Applicant has amended claim 1 to recite the compounds exemplified in the specification, which are isoquinoline-3-carboxylic acid {(1-azabicyclo[2.2.2]oct-3-yl)}-amides in which the isoquinoline moiety is either unsubstituted or mono-substituted at the 6 or 8 position with a fluoro group<sup>1</sup>.

None of the compounds in present claim 1 are disclosed in Jacobsen. Thus, claim 1 is novel and not anticipated by Jacobson. Because claim 5 depends from claim 1 and incorporates all of its elements, claim 5 is also novel and not anticipated.

Claims 1, 3-5, and 8-11 are also rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Corbett *et al.*, Pub. No. US 2005/0245504 (“Corbett”), Rogers *et al.*, Pub. No. US 2005/0107425 (“Rogers”), and Groppi *et al.*, Pub. No. US 2006/0019984 (“Groppi”). (Office Action, at page 10-12; at page 6, lines 9-11; and at page 14, lines 9-11.) For each of these references, the Office cites the same two specific isoquinoline-substituted bicyclo compounds to support of the rejection: N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-3-isoquinoline-carboxamide and its methyl derivative N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-methyl-3-isoquinolinecarboxamide. (Office Action, at pages 12-15.)

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<sup>1</sup> Applicant wishes to note that he is permitted to rely on, among other things, the contents of the inventors' laboratory notebooks to establish a date of invention prior to the apparent 102(e) date of the Jacobsen reference, in order to remove the Jacobsen. Applicant is in the process of investigating this possibility and reserves the right to reinstate the full scope of claim 1 in the future, in the event that the Jacobsen reference can be successfully antedated through establishment of an earlier date of invention.

Applicant submits that claims 1, 3-5 and 8-11 are not anticipated by Corbett, Rogers, or Groppi because none of these three references has a 35 U.S.C. § 102(e) critical reference date that is prior to Applicant's priority date of May 12, 2003 for the purposes of this rejection. Thus, these references cannot be used as prior art against Applicant's claims.

The 35 U.S.C. § 102(e) critical reference date of a U.S. patent or patent publication is the filing date of the provisional application *if* the provisional application properly supports the subject matter relied upon to make the rejection in compliance with 35 U.S.C. § 112, first paragraph. See Manual of Patent Examining Procedure (MPEP), Eighth Ed., Section 2136.03, III, at page 2100-94 (August 2007).

The provisional application relied upon by Corbett, U.S. 60/432,527, discloses a broad genus of compounds and some specific compounds, but fails to disclose either of the two compounds cited by the Examiner, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-3-isoquinoline-carboxamide and N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-methyl-3-isoquinolinecarboxamide. Each of these specific compounds is first disclosed in the subsequent non-provisional application, Appl. No. 10/731,565, which was filed on December 9, 2003. The effective 35 U.S.C. § 102(e) date for Corbett for the purposes of the rejection is thus the filing date of the nonprovisional application, December 9, 2003, which is *after* the May 12, 2003 filing date of Applicants' priority GB Appl. No. 0310867.7. Corbett cannot be used as prior art against Applicants' claims.

The same is true for both Rogers and Groppi. The provisional application relied upon by Rogers, U.S. 60/432,586, also discloses a broad genus of compounds, but fails to disclose either of the two specific compounds cited by the Office. Each compound is first disclosed in the subsequent non-provisional application, Appl. No. 10/731,402, which was filed on December 9, 2003, giving Rogers an effective 35 U.S.C. § 102(e) date of December 9, 2003, which is *after* Applicant's May 12, 2003 priority date. Rogers thus also cannot be used as prior art against Applicant's claims.

Similarly, Groppi cannot be used as prior art against the claims, because the compounds cited in the rejection are first disclosed in the nonprovisional application, Appl. No. 10/761,914, filed on January 21, 2004, rather than in priority provisional application, thus giving Groppi an effective 35 U.S.C. § 102(e) date of January 21, 2004, which is *after* Applicant's May 12, 2003 priority date.

Thus, neither Corbett, Rogers, nor Groppi can be used as prior art against claims 12-14 because the 35 U.S.C. § 102(e) critical reference date for each falls *after* Applicant's priority date of May 12, 2003. Accordingly, claims 1, 3-5 and 8-11 cannot be anticipated by these references and are thus novel over the cited references.

Applicant believes that the rejection of claims 1, 3-5, and 8-11 under 35 U.S.C. § 102 has been overcome or rendered moot and requests that this rejection be withdrawn.

### **III. Rejection of the Claims Under 35 U.S.C. § 103**

Claims 12-14 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Jacobsen *et al.*, U.S. Pat. No. 7,001,900 ("Jacobsen"). (Office Action, at page 16, lines 9-10.). Applicant respectfully traverses.

In support of the rejection, the Office cites two compounds disclosed in Jacobsen, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-chloro-3-isoquinolinecarboxamide and N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-5-chloro-3-isoquinolinecarboxamide. (Office Action, at pages 16 and 17.) According to the Office, the difference between the claimed compounds and the cited Jacobsen compounds is that the claimed compounds are substituted with a fluoro group rather than a chloro group as in the cited compounds. The Office believes that one of ordinary skill in the art would be motivated to modify the Jacobsen compounds to obtain the claimed compounds because " 'F' and 'Cl' are both halogen" and "[c]hanging one halogen to another halogen is within skill in the art." (Office Action, at page 17, lines 6-8.)

Applicant submits that, contrary to the position taken by the Office, one of ordinary skill in the art at the time of the invention, in view of Jacobsen, would not have arrived at the claimed compounds because Jacobsen fails to teach or fairly suggest compounds substituted solely with a fluoro group.

In the examples of specific compounds disclosed in Jacobsen that contain fluoro-substituted moieties, those moieties are either di-substituted with a chloro and a fluoro group (e.g., 5-chloro-4-fluoropyrimidine), or are di-substituted with a fluoro and with a fluoro-substituted alkyl group such as trifluoromethyl (e.g., 5-fluoro-4-trifluoromethylpyrimidine). See, for example, the compounds listed in columns 81-94 of Jacobsen. Moreover, of the compounds in columns 81-94 that contain a moiety mono-substituted with a halo group, in all instances the one halo group is chloro – it is not fluoro. Thus, none of the specific

compounds listed in columns 81-94 contain moieties that are directly substituted solely with a fluoro group, as in the claimed compounds. Thus, Jacobsen fails to teach or fairly suggest the claimed compounds, and may, in fact, teach away from the claimed compounds. One of skill in the art would not have been motivated to substitute a fluoro group for a chloro group in the compounds disclosed in Jacobsen to arrive at Applicants' claimed fluoro-substituted compounds.

For these reasons, Applicant believes that one of ordinary skill in the art, in view of Jacobsen, would not have been led to produce compounds containing an isoquinoline moiety substituted solely with a fluoro group such as those recited in present claims 12-14. Accordingly, claims 12-14 would not have been obvious in light of Jacobsen.

Applicant believes that the rejection of claims 12-14 under 35 U.S.C. § 103 has been overcome and requests that this rejection be withdrawn.

#### **IV. New Claims**

In this response, Applicant has added new claims 15-17. None of the references cited in the outstanding rejections that validly represent prior art teach or suggest the combination of features set forth in new independent claim 15 or the additional features of dependent claims 16 and 17 when considered in combination with claim 15.

#### **CONCLUSION**

Based on the foregoing remarks, Applicant respectfully requests that the Examiner reconsider all rejections and objections and that they be withdrawn. Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to

charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By P.D.S.

FOLEY & LARDNER LLP  
Washington Harbour  
3000 K Street NW, Suite 500  
Washington, D.C. 20007-5143  
Telephone: (202) 672-5540  
Facsimile: (202) 672-5399

Paul D. Strain  
Attorney for Applicant  
Registration No. 47,369

Ann E. Summerfield  
Attorney for Applicant  
Registration No. 47,982